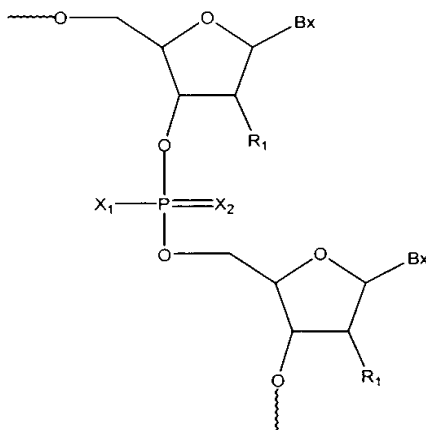


This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently amended) A method of preparing an oligomeric compound having at least one moiety of formula:



wherein:

X₂ is O or S;

X₁ is Pg-O-, Pg-S-, C₁-C₁₀ straight or branched chain alkyl, CH₃(CH₂)_{nn}-O-, R₂R₃N- or a group remaining from coupling a chiral auxiliary;

nn is from 0 to 10;

Pg is CH₃, -CH₂CH₂CN, -C(CH₃)(CH₃)-CCl₃, -CH₂-CCl₃, -CH₂CH=CH₂, CH₂CH₂SiCH₃, 2-yl-ethyl phenylsulfonate, δ-cyanobutenyl, cyano *p*-xylyl, diphenylsilylethyl, 4-nitro-2-yl-ethylbenzene, 2-yl-ethyl-methyl sulfonate, methyl-N-trifluoroacetyl ethyl, acetoxy phenoxy ethyl, or a blocking group;

R₁ is, independently, hydrogen, a blocked hydroxyl group, a sugar substituent group, a nitrogen protecting group, a substituted or unsubstituted C₁-C₁₀alkyl, a substituted or unsubstituted C₂-C₁₀ alkenyl, or a substituted or unsubstituted C₂-C₁₀alkynyl, wherein said

substitution is OR_3 , SR_3 , NH_3^+ , $N(R_3)(R_4)$, guanidine or acyl where said acyl is an acid amide or an ester;

R_2 is, independently, hydrogen, a C_1 - C_{10} alkyl, a cycloalkyl, an aryl, a nitrogen protecting group, a substituted or unsubstituted C_1 - C_{10} alkyl, a substituted or unsubstituted C_2 - C_{10} alkenyl, or a substituted or unsubstituted C_2 - C_{10} alkynyl, wherein said substitution is OR_3 , SR_3 , NH_3^+ , $N(R_3)(R_4)$, guanidine or acyl where said acyl is an acid amide or an ester;

or R_1 and R_2 together, are a nitrogen protecting group or are joined in a ring structure;

R_3 is, independently, hydrogen, a C_1 - C_{10} alkyl, a cycloalkyl, an aryl, or a nitrogen protecting group;

R_4 is, independently, $N(L_1)L_2$, hydrogen, a C_1 - C_{10} alkyl, or a nitrogen protecting group;

or R_3 and R_4 , together, are a nitrogen protecting group;

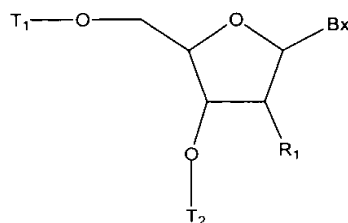
or R_3 and R_4 are joined in a ring structure;

or optionally, R_2 and R_3 , together with the nitrogen atom to which they are attached form a cyclic moiety;

each B_x is, independently, a heterocyclic base moiety; and

comprising the steps of:

(a) providing a 5'-O-protected compound of the formula:



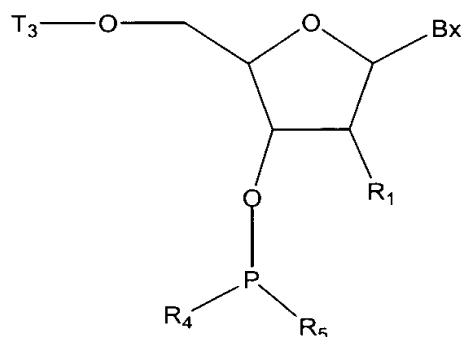
wherein:

T_1 is a hydroxyl protecting group; and

T_2 is a covalent attachment to a support media, a nucleoside bound to a support media, a nucleotide, an oligonucleoside or an oligonucleotide;

(b) treating said 5'-O-protected compound with a deprotecting reagent for a time and under conditions effective to form a 5'-O-deprotected compound;

(c) coupling said 5'-O-deprotected compound with an activated phosphorus composition of the formula:



wherein:

T_3 is a hydroxyl protecting group, a nucleoside, a nucleotide, an oligonucleoside or an oligonucleotide;

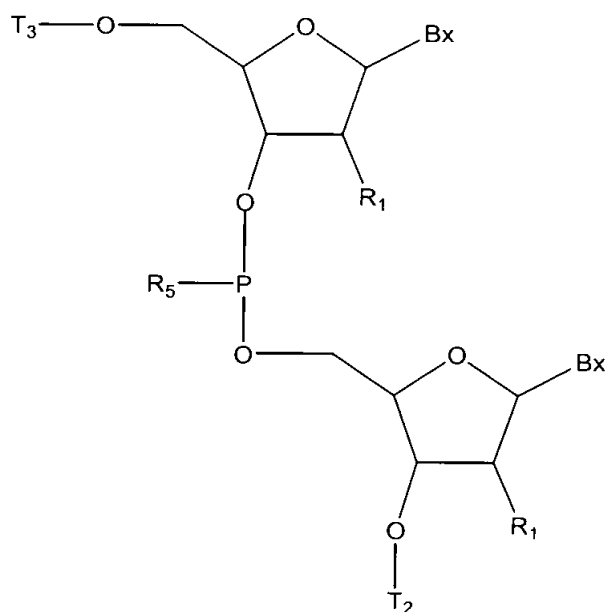
each L_1 and L_2 is, independently, C_{1-6} straight or branched alkyl, or a C_{5-7} cyclic aliphatic ring system;

or L_1 and L_2 are joined together to form a 4- to 13-membered heterocyclic ring system including the nitrogen atom to which ~~L_1 and L_2~~ L_1 and L_2 are attached; and

R_5 is X_1 ;

or R_4 and R_5 together with the phosphorus atom to which R_4 and R_5 are attached form a chiral auxiliary;

for a time and under conditions effective to form an extended compound having the formula:



(d) treating said extended compound with a mixture comprising an oxidizing reagent and a capping reagent in a single step and for a time and under conditions effective to form said oligomeric compound.

2. (Original) The method of claim 1 further comprising treating said oligomeric compound with a reagent for a time and under conditions effective to remove said blocking groups thereby forming a deblocked oligomeric compound.
3. (Original) The method of claim 2 wherein said reagent is effective to cleave the oligomeric compound from the support media.
4. (Original) The method of claim 3 wherein said reagent is aqueous ammonium hydroxide.
5. (Original) The method of claim 2 further comprising treating said oligomeric compound with a further reagent for a time and under conditions effective to cleave the oligomeric compound from the support media.
6. (Original) The method of claim 1 further comprising treating said oligomeric compound with a deprotecting reagent for a time and under conditions effective to deprotect the T₃ hydroxyl protecting group.
7. (Original) The method of claim 1 wherein said mixture comprises from 0.02M to 0.2M oxidizing reagent.
8. (Original) The method of claim 7 wherein said mixture comprises from 0.1M to 0.2M oxidizing reagent.

9. (Original) The method of claim 1 wherein said oxidizing reagent transfers an oxygen atom.

10. (Original) The method of claim 9 wherein said oxidizing reagent is iodine, *m*-chloroperbenzoic acid, iodobenzene diacetate, tetra-*n*-butylammonium periodate, *tert*-butyl hydroperoxide, di-*tert*-butyl hydroperoxide, cumene hydroperoxide, hydrogen peroxide; bis-trimethylsilyl peroxide; dinitrogen tetroxide, oxone, molecular oxygen, (1*S*)-(+)-(10-camphorsulfonyl)oxaziridine or a peracid.

11. (Original) The method of claim 10 wherein said oxidizing reagent is iodine, *m*-chloroperbenzoic acid, iodobenzene diacetate, *tert*-butyl hydroperoxide, di-*tert*-butyl hydroperoxide, hydrogen peroxide, oxone, molecular oxygen or a peracid.

12. (Original) The method of claim 1 wherein said oxidizing reagent transfers a sulfur atom.

13. (Original) The method of claim 12 wherein said oxidizing reagent is 3-amino-1,2,4-dithiazole-5-thione; 3-ethoxy-1,2,4-dithiazoline-5-one; 1,2,4-dithiazolidine-3,5-dione; 3-methyl-1,2,4-dithiazolin-5-one; or dimethylthiuram disulfide.

14. (Original) The method of claim 13 wherein said oxidizing reagent is dimethylthiuram disulfide.

15. (Original) The method of claim 1 wherein said capping reagent comprises about one part by volume of either acetic anhydride in acetonitrile or tetrahydrofuran; or chloroacetic anhydride in acetonitrile or tetrahydrofuran; added to about one part by volume of either N-methylimidazole and pyridine in acetonitrile or tetrahydrofuran; or *t*-butylphenoxyacetic anhydride in acetonitrile or tetrahydrofuran.

16. (Original) The method of claim 15 wherein said capping reagent comprises about one part by volume of 20% acetic anhydride in acetonitrile mixed with about one part by volume of a solution having 20% N-methylimidazole, 30% pyridine and 50% acetonitrile.

17. (Original) The method of claim 1 wherein said mixture comprises dimethylthiuram disulfide, acetic anhydride, acetonitrile, N-methyl imidazole and pyridine.

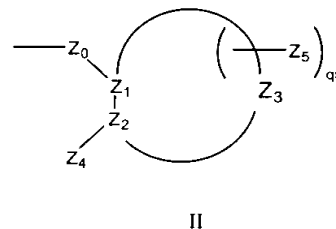
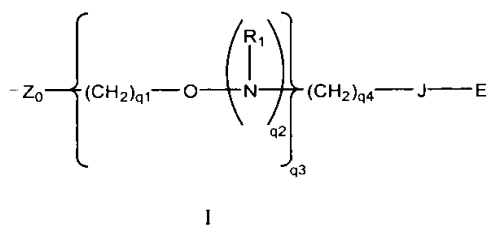
18. (Original) The method of claim 1 wherein said mixture comprises from about 0.05M to 0.2M dimethylthiuram disulfide, about 10% acetic anhydride, about 10% N-methyl imidazole and about 15% pyridine in a suitable solvent.

19. (Original) The method of claim 18 wherein said solvent is acetonitrile, toluene, ethyl acetate, tetrahydrofuran, dichloromethane, dichloroethane, dioxane, dimethylacetamide and dimethylformamide.

20. (Original) The method of claim 1 wherein said coupling of the 5'-O-deprotected compound with the activated phosphorus composition is performed in the presence of an activating agent.
21. (Original) The method of claim 20 wherein said activating agent is 1-H-tetrazole or 4,5-dicyanoimidazole.
22. (Original) The method of claim 1 where said cyclic moiety is morpholino or phthalimido.
23. (Original) The method of claim 1 wherein each L_1 and L_2 is C_{1-6} alkyl.
24. (Original) The method of claim 23 wherein each L_1 and L_2 is isopropyl.
25. (Original) The method of claim 1 wherein L_1 and L_2 are joined together to form a heterocyclic ring system including the nitrogen atom to which said L_1 and L_2 are attached, wherein said ring system optionally includes at least one additional heteroatom selected from O, N and S.
26. (Original) The method of claim 25 wherein said heterocyclic ring system is morpholino.

27. (Currently amended) The method of claim 1 wherein each of said sugar substituent groups is, independently, C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₅-C₂₀ aryl, O-alkyl, O-alkenyl, O-alkynyl, O-aryl, O-aralkyl, O-alkylamino, O-alkylaminoalkyl (O-alkyl-N(H)alkyl), O-alkylaminodialkyl (O-alkyl-N-(alkyl)₂), O-alkylalkoxy (O-alkyl-O-alkyl), O-alkyl-(N-imidazole), thiol, S-alkyl, S-alkenyl, S-alkynyl, NH-alkyl, NH-alkenyl, NH-alkynyl, N-dialkyl, S-aryl, NH-aryl, S-aralkyl, NH-aralkyl, N-phthalimido, halogen keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, N-imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, heterocycle, carbocycle, polyamine, polyamide, polyalkylene glycol, or polyether;

or, alternatively, one or more substituent groups has one of formula I or II:

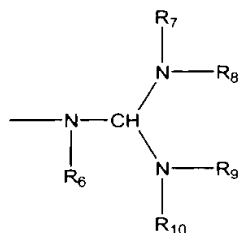


wherein:

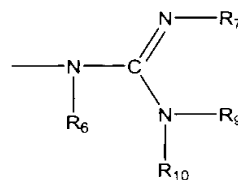
Z₀ is O, S or NH;

J is a single bond, O or C(=O);

E is C₁-C₁₀ alkyl, N(R₁)(R₂), N(R₁)(R₅), N=C(R₁)(R₂), N=C(R₁)(R₅) or has one of formula III or IV;



III



IV

each R₆, R₇, R₈, R₉ and R₁₀ is, independently, hydrogen, C(O)R₁₁, substituted or unsubstituted C₁-C₁₀ alkyl, substituted or unsubstituted C₂-C₁₀ alkenyl, substituted or unsubstituted C₂-C₁₀ alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group or a conjugate group, wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl;

or optionally, R₇ and R₈, together form a phthalimido moiety with the nitrogen atom to which they are attached;

or optionally, R₉ and R₁₀, together form a phthalimido moiety with the nitrogen atom to which they are attached;

each R₁₁ is, independently, substituted or unsubstituted C₁-C₁₀ alkyl, trifluoromethyl, cyanoethoxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl or aryl;

R₅ is T-L,

T is a bond or a linking moiety;

L is a chemical functional group, a conjugate group or a support media;

each R₁ and R₂ is, independently, H, a nitrogen protecting group, substituted or unsubstituted C₁-C₁₀ alkyl, substituted or unsubstituted C₂-C₁₀ alkenyl, substituted or

unsubstituted C₂-C₁₀ alkynyl, wherein said substitution is OR₃, SR₃, ~~NH₃~~ \neq $\underline{\text{NH}_3^+}$, N(R₃)(R₄), guanidino or acyl where said acyl is an acid amide or an ester;

or R₁ and R₂, together, are a nitrogen protecting group or are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

or R₁, T and L, together, are a chemical functional group;

each R₃ and R₄ is, independently, H, C₁-C₁₀ alkyl, a nitrogen protecting group, or R₃ and R₄, together, are a nitrogen protecting group;

or R₃ and R₄ are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

Z₄ is OX, SX, or N(X)₂;

each X is, independently, H, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C(=NH)N(H)R₅, C(=O)N(H)R₅ or OC(=O)N(H)R₅;

R₅ is H or C₁-C₈ alkyl;

Z₁, Z₂ and Z₃ comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

Z₅ is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, N(R₁)(R₂) OR₁, halo, SR₁ or CN;

each q₁ is, independently, an integer from 1 to 10;

each q₂ is, independently, 0 or 1;

q₃ is 0 or an integer from 1 to 10;

q_4 is an integer from 1 to 10;

q_5 is from 0, 1 or 2; and

provided that when q_3 is 0, q_4 is greater than 1.

28. (Original) The method of claim 1 wherein said X_1 is Pg-O-, Pg-S-, CH₃-, CH₃-O-, morpholino or R₂R₃N- where each R₂ and R₃ is, independently, hydrogen or C₁-C₁₀ alkyl.

29. (Original) The method of claim 1 wherein said Pg is CH₂CH₂CN, diphenylsilylethyl, δ -cyanobutenyl, cyano p-xylyl, methyl-N-trifluoroacetyl ethyl or acetoxo phenoxy ethyl.

30. (Original) The method of claim 1 wherein said heterocyclic base moiety is adenine, N⁶-benzoyladenine, cytosine, N⁴-benzoylcytosine, 5-methylcytosine, N⁴-benzoyl-5-methylcytosine, thymine, uracil, guanine, N²-isobutyrylguanine or 2-aminoadenine.

31. (Original) The method of claim 1 wherein said support media bound nucleoside, nucleotide, oligonucleoside or oligonucleotide is blocked at reactive sites.

32. (Original) The method of claim 1 wherein said blocking groups are acid stable.

33. (Original) The method of claim 1 wherein said blocking groups are base labile.

34. (Original) The method of claim 1 wherein said deprotecting reagent is acidic, neutral or basic.

35. (Previously amended) The method of claim 34 wherein said deprotecting reagent is dichloroacetic acid, trichloroacetic acid, zinc bromide, AlCl_3 , TiCl_4 , $(\text{Et})\text{AlCl}$, $(i\text{-Bu})_2\text{AlCl}$, ceric ammonium nitrate, 1,1,1,3,3,3-hexafluoro-2-propanol or diethyloxomalonate.

36. (Original) The method of claim 35 wherein said deprotecting reagent is 2-5% dichloroacetic acid in dichloromethane or dichloroethane.

37. (Original) The method of claim 1 wherein said deprotecting reagent is a fluoride moiety.

38. (Original) The method of claim 37 wherein said fluoride moiety is BF_3 -etherate.

39. (Original) The method of claim 1 wherein said oligomeric compound comprises from 5 to about 50 nucleosides.

40. (Original) The method of claim 1 wherein said oligomeric compound comprises from 8 to about 30 nucleosides.

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41. (Original) The method of claim 1 wherein said oligomeric compound comprises from 15 to about 25 nucleosides.